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CORRESPONDENCE

Research Correspondence

Subacute Coronary Stent Thrombosis in Cancer Patients

To the Editor: In-stent thrombosis (IST) remains a major challenge in interventional cardiology. Trials comparing balloon angioplasty with coronary stenting demonstrated an IST incidence >5% (1,2). Improved stent deployment combined with dual antiplatelet therapy reduced the incidence to 0.5% to 2% (3–6). Aside from appropriate antiplatelet therapy, high-pressure balloon inflation, optimal lumen diameter, the absence of proximal or distal flow-limiting lesions, and endothelial stent surface restoration, are all believed to protect against IST (7). Factors that increase IST risk include long stents, stent malapposition, residual dissections, and aspirin or thienopyridine resistance (8). Although malignancy is associated with venous thrombosis, little is known about increased IST in cancer patients (9). Because cancer patients are now commonly referred, we tested the notion that cancer would increase the risk for IST. We reviewed the hospital records of all patients undergoing bare-metal stenting between January 1997 and May 2007. We identified IST patients and cancer in our computerized database. We then reviewed the angiograms and medical records. Patients who received drug-eluted stents or who underwent left main stem stenting were excluded. Angiographic criteria of stent thrombosis were partial or complete occlusion. We expressed continuous data as mean ± SD. We expressed discrete variables as counts or percentages with chi-square analysis. We conducted group comparisons for continuous data with unpaired 2-sided *t* tests.

Table 1 summarizes the demographic and clinical characteristics of the patients. We found 108 patients with cancer; IST occurred in 55 of 7,081 patients without known malignancies (0.78%) and in 6 of 108 cancer patients (5.56%; chi-square = 26.86, $p < 0.000001$, odds ratio 7.10, 95% confidence interval 2.70 to 17.61). Median time to IST was 7 days in cancer patients versus 4 days in control subjects. In patients without malignancies, the culprit lesions were located in the left anterior descending coronary artery (LAD) in 40%, the left circumflex coronary artery (LCX) in 31%, and the right coronary artery (RCA) in 30%. The corresponding vessels in the 6 cancer patients with IST were 3 in the LAD, 1 in the LCX, and 2 in the RCA, although the numbers are too small to identify any one vessel. One patient in each group had discontinued the recommended dual antiplatelet therapy. Because IST is associated with stent size, we compared stent diameter and length. The average stent diameter was 2.67 ± 0.26 mm ($p = 0.85$) in cancer patients versus 2.64 ± 0.50 mm (p = NS) in controls. However, there was a tendency to implant shorter stents in the cancer patients; the average stent length was 18.30 ± 0.26 mm ($p = 0.06$) versus 20.90 ± 0.29 mm (p = NS) in the control group. The stenting procedures were elective in 56% of controls, compared with 50% in cancer patients. Notably, all 6 IST cancer patients had solid tumors; none had leukemia, lymphoma, or multiple myeloma. The tumors were 3 lung cancers, 1 cervical cancer, 1 breast cancer, and 1 colon cancer.

This brief retrospective survey supported our clinical impression that cancer patients have more IST than expected. The issue is important because cardiological advances coupled with improved prognosis for cancer patients will increase the patient number accordingly. Furthermore, clinicians understand that many cancer patients have a better prognosis than heart failure or renal failure patients. Thus, the numbers of cancer patients receiving cardiovascular interventions will increase.

Cancer is an acquired thrombophilic condition (10). Thus, increased IST in cancer patients should not evoke surprise. Cancer patients commonly present with a hypercoagulable state, even in the absence of thrombosis. Furthermore, clotting activation may play a role in tumor progression. The pathogenesis of thrombosis in cancer is multifactorial; however, a relevant role is attributed to the tumor cell capacity to interact with and activate the host hemostatic system. The prothrombotic action of antitumor therapies is also important. Thrombotic events can influence the morbidity and mortality of the underlying disease.

Table 1 Demographic and Clinical Parameter of the Patients

	CAD (n = 7,081)		CAD With Concomitant Malignant Disease (n = 108)	
	No IST (n = 7,026)	IST (n = 55)	No IST (n = 102)	IST (n = 6)
Age, yrs, male/female	62.9 ± 10.6/68.0 ± 10.5	63.0 ± 12.2/63.8 ± 8.5	67.0 ± 11.3/67.0 ± 8.8	70.0 ± 6.7/76.0 ± 5.7
Gender, male (%)	5,241 (74.6)	39 (70.9)	84 (82.4)	4 (66.7)
Diabetes mellitus, n (%)	1,613 (23.0)	14 (25.4)	21 (20.6)	1 (16.7)
Hypertension, n (%)	4,497 (64.0)	28 (50.9)	52 (51.0)	3 (50.0)
Hypercholesterolemia, n (%)	3,510 (50.0)	27 (49.1)	37 (36.3)	3 (50.0)
Aspirin, n (%)	5,690 (81.0)	44 (80.0)	83 (81.4)	4 (66.7)
Clopidogrel, n (%)	4,545 (64.70)	37 (67.3)	71 (69.6)	5 (83.3)
Ticlopidine, n (%)	1,370 (19.5)	14 (25.5)	11 (10.9)	1 (16.7)
Phenprocoumon, n (%)	689 (9.8)	7 (12.7)	6 (5.9)	1 (16.7)

CAD = coronary artery disease; IST = in-stent thrombosis.

Preventing thrombotic complications in cancer patients is highly relevant above-and-beyond IST. New approaches in cancer patients have been investigated and the hypothesis that strategies to inhibit clotting mechanism may favorably affect malignant disease is gaining interest. Evidence-based strategies are being developed to treat cancer patients with venous thromboembolism. Phenprocoumon (warfarin and derivates) is problematic in cancer patients because of unpredictable responses and variable efficacy. Hull et al. (11) recently reported a multicenter, randomized, open-label clinical trial using objective outcome measures comparing long-term therapeutic low molecular weight heparin subcutaneously to warfarin therapy in cancer patients. Bleeding complications were the same. However, 16% of the warfarin group developed thrombosis recurrence, compared with 7% in the low-molecular-weight heparin group.

We are uncertain how stented cancer patients should be best treated. Five of 6 developed IST despite optimal antiplatelet therapy. Whether or not these patients should receive subcutaneous low molecular weight heparin, as did the cancer patients in the trial by Hull et al. (11), is unknown. We pose the question of how cancer patients will respond to drug-eluting stents. These stents behave differently to endothelial repair. We have not placed such stents in cancer patients. Consideration could also be given to treat such high-risk patients with balloon dilatation alone without stenting. Surveillance studies are necessary to address this important question.

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Letters to the Editor

Debating About a Registry to Define the Best Invasive Treatment for Obstructive Hypertrophic Cardiomyopathy

Should It Also Include Obstructive Patients Medically Treated?

We have read with great interest the Viewpoint by Olivotto et al. (1) that recently was published in the *Journal*. The authors have convincingly demonstrated that a randomized prospective trial comparing the results of these 2 techniques is not feasible, because it would require the enrollment of more than 30,000 patients with hypertrophic cardiomyopathy. We agree with their conclusion that this issue can only be addressed by a large international multicenter registry.

However, in our opinion, the discussion on the respective advantages of surgical myectomy and alcohol septal ablation should not distract from the crucial and, still controversial, question of which patients are appropriate candidates for the myectomy operation. Indeed, the international guidelines on hypertrophic cardiomyopathy define candidates to myectomy as "both adults and children with obstructive hypertrophic cardiomyopathy and severe drug-refractory symptoms" (2). On the other hand, 2 recent